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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/550,165

07/21/2006

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0179689010-US00

5240

23510 7590 10/27/2008  
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EXAMINER

KRISHNAN, GANAPATHY

ART UNIT

PAPER NUMBER

1623

MAIL DATE

DELIVERY MODE

10/27/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/550,165	<b>Applicant(s)</b> SAVAGE ET AL.	
	<b>Examiner</b> Ganapathy Krishnan	<b>Art Unit</b> 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-13, 18, 19, 24 and 25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13, 18, 19, 24 and 25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/15/2008</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

The amendment filed 7/8/2008 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 14-17, 20-23 have been canceled.
2. Remarks drawn to rejections under 35 USC 103

Claims 1-13, 18-19 and 24-25 are pending in the case.

### ***Specification***

The objection to the abstract advanced in the previous action is being maintained. Applicants have not responded to this objection.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of Claims 1-13, 18-19 and 24-25 under 35 U.S.C. 103(a) as being unpatentable over Tsuji et al (US 7273852; priority of provisional application Jan.13, 2002) in view of Defrees et al (US 5,604,207), Sinay et al (Bioorganic and Medicinal Chemistry, 1998, 6, 1337-46) and Kawano et al (Science, 1997, 278, 1626-29); document cited in IDS of 5/25/2007) is being maintained for reasons of record.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicants have traversed the rejection arguing that:

1. Tsuji teaches C-sugar linkages, which has to be replaced by an O-linkage. Such O-linked sugars are taught by Tsuji to have short half life and their in vivo therapeutic effects may be reduced. C-linked compounds have improved stability and are more potent than O-linked compounds.

2. The O-linked compounds are not within the scope of the claims or described as the invention.

3. According to Kawano's teaching activity cannot be predicted from structure. Because of this there cannot be a reasonable expectation of success.

Applicants' arguments have been considered but are not found to be persuasive.

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Tsuji teaches that the short half life and therapeutic effects may be reduced. This disclosure of Tsuji means that he is not sure that the therapeutic effects will definitely be reduced or will be totally eliminated on replacing the C-linkage with an O-linkage. Structure KRN 7000 according to Tsuji shows activity against tumors in mice and preventing cancer metastasis. And alphaGalCer is not cytotoxic to humans (see col. 5, lines 5-30). AlphaGalCer are also display other activities such as immunostimulating agents, antimicrobial and antivirals (col. 3, line 25 through col. 4, line 45). Various structural modifications are also suggested. This teaching is motivation to look for other similar compounds that have enhanced activities. In instant formula (I) the lipid moiety is linked through an oxygen to the anomeric carbon of the sugar. It is an O-linked compound. This is the type of compound that is taught by Tsuji in the columns and lines pointed out above. Tsuji also suggests substituted amino sugar moieties (col. 3, lines 55-60). Even though the amino unit is not at the C-6 position one of skill in the art has to move it to that location to determine its activity as part of an optimization/structure-activity study. Such is routine in the art.

Kawano et al, drawn to activation of NKT cells, teach that fatty acyl chains in combination with galactosyl moiety (GalCer) are important for selective activation of NKT cells and it is these cells that kill target tumor cells by an NK like mechanism and inhibit tumor growth and metastasis (page 1628, left column, last paragraph and middle column, first full paragraph). It is true that activity cannot be predicted on an absolute basis. But just because Kawano discloses different activities for structural variations does not mean that one of skill in the art would not pursue such modifications. The genus of Kawano (page 1627, right column) is not very huge. In such structure-activity studies as reported by Kawano one of ordinary skill in

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the art would expect some compounds to show reduced activity. This is actually motivation to keep looking for other similar compounds that show enhanced activity. This is how the art advances. When the core structural features have interesting biological activity structural modifications within the core to generate new derivatives with enhanced activity is routine in medicinal chemistry.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the compounds of formula I, their compositions and use them in a method to stimulate NKT cells and make the said compounds via the process as instantly claimed since such is seen to be taught in the prior art using closely analogous compounds. It is well within the skill level of the artisan to apply the same conversion steps to the compound as instantly claimed in claims 24-25.

One of skill in the art would be motivated to make the compounds and their compositions as instantly claimed since closely analogous compound have been shown to be good stimulators of NKT cells (taught by both Tsuji and Kawano), which are known to inhibit tumor growth and metastasis. Hence one of skill in the art would look for structurally related compounds that are more potent inhibitors. Obviousness based on similarity of structure and function entails motivation to make the claimed compound in expectation that compounds similar in structure will have similar properties. Where prior art compound essentially brackets the claimed compounds and are well known active agents for the intended purpose, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new anticancer/antitumor agents. In re Payne, 606 F. 2d 303, 203, USPQ, 245, 254-55 (C.C.P.A. 1979). Applicants have not addressed the rejection of method claims 24-25.

***Conclusion***

Claims 1-13, 18-19 and 24-25 are rejected.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/

Examiner, Art Unit 1623